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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/708,204	02/16/2004	Itzhak Bentwich	050992.0201.03USCP	2203
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ROSETTA-GENOMICS c/o POLSINELLI SHUGHART PC 700 W. 47TH STREET SUITE 1000 KANSAS CITY, MO 64112			EXAMINER WOLLENBERGER, LOUIS V	
			ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/708,204	Applicant(s) BENTWICH, ITZHAK	
	Examiner Louis Wollenberger	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 April 2010 and 19 April 2010.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 31, 32 and 39-42 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 31 and 39 is/are allowed.
- 6) ☒ Claim(s) 32 and 40-42 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on 4/17/2010 and 4/19/2010 have been entered.

Status of Application/Amendment/Claims

Applicant's responses filed 4/17/2010 and 4/19/2010 have been considered. Rejections and/or objections not reiterated from the previous office action mailed 1/26/2010 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

Also acknowledged are applicant's amendments to the claims filed 4/17/2010 and 4/19/2010. With entry of the amendments, claims 31, 32, and 39-42 are pending and examined herein.

Priority

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c), and 35 U.S.C. 119(a)-(d) is acknowledged.

To obtain the benefit of a prior filed application, the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the

invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

In the instant case the disclosures of prior-filed Application Nos. 60/468,251, 10/649,653, 10/651,227, 10/707,147 11/24/2003, 10/604,985, 10/604,926, 10/604,727, 10/604,726, 10/707,975, 10/707,980, and PCT/IL03/00998 fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for claims 31, 32, and 39-42. Specifically, written description support for DNAs encoding SEQ ID NO:6527 and 15 and any complements of these DNAs or RNA sequences is not readily identified in prior filed Application 10/707147 or any other prior filed application to which priority is now claimed. Further, written description support is not found for vectors comprising any of these RNA or DNA sequences or for oligonucleotide probes 16-140 nucleotides in length comprising SEQ ID NO:15 or 6527 or any DNA sequence or complement thereof, as now claimed.

In a previous reply, Applicant stated and the Examiner noted instant SEQ ID NO:15 and 6527 are identical to SEQ ID NO:303 and 169, respectively, in Application No. 10/707,147, filed 11/24/2003. However, claims 31 and 32 are not limited to just these sequences but include DNAs encoding these sequences as well as the complements thereof. Applicant has not pointed out how these sequences are supported by prior filed application 10/707147, nor how the genus of oligonucleotide probes 16-140 nucleotides in length comprising these sequences are supported by prior filed application 10/707147.

Accordingly, for purposes of this examination the earliest effective filing date of claims 31, 32, and 39-42 is considered to be that of the instant application: 2/16/04.

Claim Rejections - 35 USC § 112, first paragraph (new matter)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 41 and 42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Adequate written description support is not found in the instant application for the genus of oligonucleotide probes 16-140 nucleotides in length comprising any of the disclosed nucleic acid sequences. Instead, written description support is found for oligonucleotide probes 16-120 nucleotides in length. See paragraphs 46 and 288, for example.

MPEP 2163, Section II, Part A, states in part that there is a strong presumption that an adequate written description of the claimed invention is present in the specification as filed, *Wertheim*, 541 F.2d at 262, 191 USPQ at 96; however, with respect to newly added or amended claims, applicant should show support in the original disclosure for the new or amended claims. The purpose of the written description requirement is "to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him." MPEP 2138.05, I. To comply with the written description requirement of 35 U.S.C. 112, para. 1, or to be entitled to an earlier priority date or filing date under 35 U.S.C. 119, 120, or

365(c), each claim limitation must be expressly, implicitly, or inherently supported in the originally filed disclosure (MPEP 2163).

In the instant case, in the remarks filed 4/17/2010 and 4/19/2010 Applicant points to paragraphs 43-46 and 53 as support for Applicant's claim to the genus of oligonucleotides 16-140 nts in length comprising SEQ ID NO:15 and 6527. However, neither these passages nor any other section of the application explicitly, implicitly, or inherently represents to one of ordinary skill in the art that applicant was in possession of the genus of oligonucleotide probes 16-140 nucleotides in length comprising each of the over 7000 nucleic acid sequences disclosed in the application at the time of filing. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997). Paragraph 46, for example, does not literally describe or imply oligonucleotide probes 16-140 nts in length. See below. Instead, the paragraph teaches that "An Oligonucleotide" is 2-139 or preferably 16-120 nucleotides. Applicant is not claiming a polynucleotide probe and there is no additional disclosure readily identifiable suggesting applicant appreciated or contemplated oligonucleotide probes or, for that matter, polynucleotide probes 16-140 nts comprising any of the over 7000 nucleic acid sequences shown in the sequence listing.

[0046] An Oligonucleotide is defined as a nucleic acid comprising 2–139 nucleotides, or preferably 16–120 nucleotides. A Polynucleotide is defined as a nucleic acid comprising 140–5000 nucleotides, or preferably 140–1000 nucleotides.

Accordingly, the instant claims as a whole are rejected for lack of written description support because one of skill would not recognize applicant was in possession of the oligonucleotide probes 16-140 nucleotides in length now claimed at the time of filing. Should Applicant disagree with the finding, Applicant is invited to point out with particularity where and how written description support may be found in the original application.

Claim Rejections - 35 USC § 102—maintained

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 32, 40, and 42 remain rejected under 35 U.S.C. 102(e) as being anticipated by Tuschl et al. (WO 03/029459) “MicroRNA molecules.”

Claim 32 is drawn to a mature, 22-nucleotide miRNA, the DNA encoding the miRNA, and all complements thereof. A search of the miRNA registry (miRBase, www.mirbase.org)

shows SEQ ID NO:15 corresponds to miR-151. The full sequence of SEQ ID NO:151 is shown below. Claims 40 and 42 are drawn to vectors and probes comprising any of the 22-nucleotide sequences defined by claim 32.

Tuschl et al. disclosed the 22-nucleotide ribonucleic acid sequence (SEQ ID NO:179) of the mature mouse miR-151 (see Table 3, page 33; reproduced in part below). The sequence is 90% identical to instant SEQ ID NO:15, differing by only two nucleotides (underlined).

20	miR-151	CUAGACUGA <u>AGC</u> UCCUUGAGGA
		(SEQ ID NO:179)

Instant SEQ ID NO:15: cuagacugaagcuccuugagga

Tuschl et al. taught that mature miRNAs have a length of 19-24 nucleotides, but in particular are 21, 22, or 23 nucleotides long (pg. 3). Tuschl et al. further taught and claimed any nucleotide sequence identical or complementary to any of the sequences disclosed in Table 3, which Table includes the mouse miR-151 sequence, SEQ ID NO:179. Tuschl et al. state their invention includes any sequence at least 80%, 90%, 95%, or 99% identical to the disclosed miRNA, SEQ ID NO:179, or its complement (pages 2 and 43). The sequences may be RNA or DNA (page 3). Accordingly, Tuschl et al. expressly contemplated (and therefore disclosed) every 22-nucleotide nucleic acid sequence that is 90% identical and complementary to the miR-151 disclosed therein at Table 3, shown above, including every DNA sequence encoding each possible 22-nucleotide sequence in this genus (see page 2 for example). Thus, Tuschl et al. described every 22-mer differing from SEQ ID NO:179 by two nucleotides. It is understood by those in the art that each position in the linear 22-nucleotide ribonucleic acid sequence is A, C, G, or U. Thus the identity of each nucleotide at each position is defined and limited to one of four possible nucleotides. Further, the relation of each nucleotide one to the other is restricted to

an unchanging linear (non-branched) nucleic acid sequence 22 nucleotides in length.

Accordingly, Tuschl et al. had described each of the various permutations here involved as fully as if they had written out each sequence (MPEP 2103.02). The list so generated is necessarily finite since the length of the miRNA and alternative (A, C, G, U) nucleobases is limited and fully defined. One of skill could therefore immediately envision each sequence and write each sequence in full.

This disclosed list of sequences necessarily includes the instantly claimed nucleic acid sequence, SEQ ID NO:15, and its complement.

At pages 4-5, Tuschl et al. taught vectors comprising these sequences. At page 21 it is taught that miRNAs are highly conserved and that almost every miRNA cloned from mouse was also encoded in the human genome. Tuschl et al. expressly recommend cloning, sequencing, and detecting miRNAs in vertebrate and invertebrates using known techniques and those disclosed therein to investigate miRNA function.

In view of this disclosure, one of skill would instantly recognize each 22-nucleotide sequence 90% identical and complementary to the mouse miR-151 shown in Table 3 as fully as if each sequence was written out. This list of sequences necessarily includes instant SEQ ID NO:15 and its complements as well as DNA sequences encoding SEQ ID NO:15. These sequences are also indistinguishable from the instantly claimed probes.

Thus, Tuschl et al. anticipates the claimed nucleic acids.

Response to Arguments

Applicant's arguments filed 4/17/2010, traversing the instant rejection over Tuschl et al. (WO 03/029459), are essentially analogous to those filed 11/23/2009. The arguments have been fully considered but are not persuasive.

A genus does not always anticipate a claim to a species within the genus. However, when the species is clearly named, the species claim is anticipated no matter how many other species are additionally named (MPEP 2131.02, citing *Ex parte A*, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990)).

When the compound is not specifically named, but instead it is necessary to select portions of teachings within a reference and combine them, e.g., select various substituents from a list of alternatives given for placement at specific sites on a generic chemical formula to arrive at a specific composition, anticipation can only be found if the classes of substituents are sufficiently limited or well delineated. *Ex parte A*, 17 USPQ2d 1716 (Bd. Pat. App. & Inter. 1990). If one of ordinary skill in the art is able to "at once envisage" the specific compound within the generic chemical formula, the compound is anticipated. One of ordinary skill in the art must be able to draw the structural formula or write the name of each of the compounds included in the generic formula before any of the compounds can be "at once envisaged." One may look to the preferred embodiments to determine which compounds can be anticipated. *In re Petering*, 301 F.2d 676, 133 USPQ 275 (CCPA 1962).

The Examiner maintains the disclosure of Tuschl et al. conforms to the standards and guidelines set out in MPEP 2103.02 for anticipation of a species.

Applicant argues the Examiner selects and combines portions of teachings in the Tuschl et al. disclosure. This argument is not persuasive because there is no prohibition against selecting portions of a disclosure when evaluating references for their anticipation of a composition. Further, like any publication, WO 03/029459, is relevant for all it contains and for all that it would have reasonably suggested to one having ordinary skill in the art (MPEP 2123 and 2128).

Applicant argues the genus disclosed by Tuschl et al. is large and that one of ordinary skill could not write down each of the sequences and therefore could not “at once” envision each sequence, including SEQ ID NO:15. This argument is not persuasive for the reasons given in the previous Action, reiterated herein. Tuschl et al. provide a list of miRNA sequences and succinctly disclose and claim nucleic acid molecules, 18-25 nucleotides in length that are 90% identical to any of these sequences. See claims 1-6 and pages 2 and 3. Tuschl et al. state that miRNAs are 21, 22, or 23 nucleotides in length (page 3). Tuschl et al. disclosed a linear, non-branched RNA sequence 22-nts in length that differs from instant SEQ ID NO:15 by two nucleotides. It is understood in the art that each nucleotide position is A, C, G, or U. Accordingly, one of skill could write each sequence, by hand or with computer assistance without hesitation or resorting to assumptions. The genus is not infinite and each sequence in the genus is in fact defined by the description in Tuschl et al. as fully as though each sequence had been written out. Tuschl et al. succinctly describes each sequence by words rather than by structural formula.

In the instant case, Tuschl et al. expressly described a nucleotide sequence having an identity of at least 90% to any sequence shown in Table 3 therein (see claims and page 2). Table 3 lists SEQ ID NO:179, a 22-nucleotide sequence that is 90% identical to instant SEQ ID NO:15 (having 20 of 22 nucleotides in common). Given that the RNA bases at each position can only be U, C, G, or A, one of skill would instantly have envisioned every 22-nucleotide sequence that is at least 90% identical to (i.e., that has at least 20 bases in common with) SEQ ID NO:179. There is no ambiguity with regard to the complete 22-nucleotide sequence or need to consider any other variable in order for one to envision each sequence expressly disclosed by Tuschl et al.—

the substituents at each position are sufficiently limited and well delineated. One of skill would have been able to write each sequence in the list of sequence 90% identical to SEQ ID NO:179. Therefore, Tuschl et al. had described each of these 22-nucleotide sequences as fully as if they had written each sequence. There is no need to write out each sequence, since the express description in Tuschl et al. concisely discloses each sequence contemplated by Tuschl et al. for inclusion in their invention.

Applicant has previously stated a genus does not anticipate a species within the genus, citing *Bristol-Myers Squibb Co. v. Ben Venue Laboratories Inc.* However, this case is not precedential and the facts therein are not analogous to those of the instant application. Here, there is no vague allegation that one of skill would recognize the claimed sequence based on general knowledge in the prior art. Instead, the rejection relies on a single reference, Tuschl et al., which expressly taught that their invention included every sequence that is at least 90% identical to the disclosed 22-mer, SEQ ID NO:179. One of skill would have envisioned each 22-nucleotide sequence on that list without having to consult any other reference.

Applicant supplies a calculation of the number of possible sequences disclosed by Tuschl et al., and states Tuschl et al. discloses nearly 200 million nucleic acids. However, this argument only substantiates the rejection, showing that, indeed, the list is necessarily finite and defined, otherwise how could one even presume to enumerate the number of sequences. The comprehensiveness of the listing does not negate the fact that the compound claimed was specifically taught. The Examiner finds no guidelines in the MPEP or case law setting cutoffs for the number of species or time it may take one of skill to write or envision each species. Such arguments would therefore appear to be arbitrary.

Moreover, the idea of “choices” is not germane to anticipation. There is no need to show one of skill would have had to pick or choose from the list, but simply that one of skill could have envisioned each sequence on the list, and that the list necessarily includes the sequence now claimed. Applicant does not dispute the fact that the list of sequences includes any of those claimed by applicant. Further, Applicant provides no evidence to show one of skill could not have envisioned each sequence on the list disclosed by Tuschl et al. based on the express language therein, succinctly describing each sequence.

Furthermore, the instant claims require no function. The claims are drawn simply to an isolated nucleic acid selected from the group consisting of SEQ ID NO:15, the DNA encoding SEQ ID NO:15, and any complements thereto. Tuschl et al. disclosed all such sequences.

Finally, it is noted that previously Applicant himself had claimed a genus of sequences “at least 80% identical to SEQ ID NO:15 and 6527” even though the instant application as filed does not, in fact, list or expressly write out each such sequence. See claims filed 2/16/2004 and 11/22/2006. Presumably the position of applicant at the time such claims were presented was that all such sequences were adequately described by their specification in the manner required by 35 USC 112, first paragraph. In this regard, the disclosure of Tuschl et al. is commensurate with Applicant's, and is no less descriptive. Indeed, in WO/03/029459, Tuschl et al., like Applicant, also claimed all sequences at least 80% identical to any of those shown in Table 3 therein.

Further, Applicant himself is also claiming an extremely large genus of oligonucleotides 16-140 nucleotides in length comprising SEQ ID NO:15. Applicant also relies on selecting and combining portions of their disclosure to find support for and demonstrate possession of each of these sequences. Tuschl et al. had described several species within this

claimed genus, more than amply describing and anticipated the claimed genus. A generic claim cannot be allowed to an applicant if the prior art discloses a species falling within the claimed genus (MPEP 2131.02).

Accordingly, the rejection of the claims as being anticipated by Tuschl et al. is maintained.

Claims 32, 40, and 42 are rejected under 35 U.S.C. 102(e) as being anticipated by Croce et al. (US 2006/0105360).

Croce et al. disclosed an hsa-mir-151 precursor and mature deoxyribonucleic acid sequences comprising instant SEQ ID NO:15. See page 45 in U.S. Provisional Application 60/543119. Croce et al. also taught that the miR sequences therein may be expressed in cells from a recombinant vector (paragraph 123). The sequence and vector thereof are indistinguishable from those defined by the instant claims. One of skill would instantly recognize the RNA equivalent of the miR-151 precursor and mature DNA sequences disclosed at page 45 of the provisional application.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Louis Wollenberger whose telephone number is (571)272-8144. The examiner can normally be reached on M-F, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Fereydoun Sajjadi can be reached on 571-272-3311. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1635

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Louis Wollenberger/
Primary Examiner, Art Unit 1635
May 1, 2010